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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/791,628	03/01/2004	Benjamin G. Davis	GC571-2-C1	3111

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EXAMINER	
MEAH, MOHAMMAD Y	
ART UNIT	**PAPER NUMBER**
1652	
MAIL DATE	**DELIVERY MODE**
03/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/791,628	DAVIS ET AL.	
	Examiner	Art Unit	
	MD. YOUNUS MEAH	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5, 8--10, 12-33, 35-38,40-57* is/are pending in the application.

4a) Of the above claim(s) *30-33, 35-38,40-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 8-10,12-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election without traverse of group I: claims 1-5, 8-10,12-29 (prior claims 1-5, 8-13-10, 19-36) in their response of 11/26/2007 is acknowledged. Applicant should state in their response that they have change the numbering of the claims in their amendment from the prior set of claims.

Election/Restriction

Applicant, on date11/26/2007, elected traverse Group I (prior claims 1-5, 8-13-10, 19-36) claims 1-5, 8-10,12-29, drawn to catalytic antagonist comprising *subtilisin*-type serine hydrolase conjugated to carbohydrate for examination. Group II: claims 30-33, 35-38,40-57 (prior claims 37-40, 44-47 and 56-73 of election/restriction-office action of date 11/20/2007) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected Groups.

Priority

This application is a continuation of 09/556,466, 04/21/2000 now abandoned which claims benefit of US 60/131, 362, 04/28/1999.

Sequence compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It

is particularly noted that variety of sequences are recited in the specification without giving any sequence listing. Appropriate correction is required. See particularly 37 CFR 1.821(d).

Claim Objections

Claims 1-5, 8-10,12-29 are objected for containing non-elected subject matters. Appropriate correction is required.

Claim Rejections

35 U.S.C 112

2nd paragraph rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 -the recitation of the term " residue of 156, residue 166, residue 217, residue 222, residue 62, residue 96, residue 104, residue 107, residue 189 and residue 209 " make the claim indefinite as it is unclear what these amino acid residues are referred to as no amino acid sequence is presented in the specification either by SEQ ID number or by accession number. Therefore reference residues are undefined.

35 U.S.C 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 8-10,12-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of catalytic antagonist comprising chimeric protein comprising any *subtillsin-type* serine hydrolase conjugated through the sulfur group on a cysteine of the said hydrolase with a genus of targeting moiety (comprising any class of compounds, a few of them described in claim 17). The specification teaches the structure of only a few such chimeric proteins. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of chimeric protein. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a

precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species, which are adequately described, are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Claims 1-5, 8-10,12-29 are directed to a genus of catalytic antagonist comprising chimeric protein of any subtilisin-type serine hydrolase conjugated through the sulfur group on a cysteine of the said hydrolase with any targeting moiety molecule. The specification discloses the structure of a few such chimeric proteins comprising SBL proteases conjugated few targeting domain molecules such as carbohydrate molecules as described in FIG 1 . The specification lacks description of any additional species of chimeric proteins and identifying characteristics or properties or structure correlated with function. Moreover it is unclear how any chimeric protein comprising any subtilisin-type serine hydrolase conjugated to any undefined targeting moiety molecule approach to and then can catalyze the cleavage of

such diverse bimolecular target molecules. Therefore one of skill in the art would not recognize from the disclosure that applicants' were in possession of the claimed invention.

Applicants' are referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-5, 8-10,12-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for catalytic antagonist comprising chimeric protein of a *bacillus lentus subtillsin*-type serine hydrolase conjugated with mannose type of oligosaccharide (oligosaccharide having mannose residue) to target mannose binding lectin (such as CONA), not reasonably provide enablement for any catalytic antagonist comprising chimeric protein comprising any subtillsin-type serine hydrolase conjugated through the sulfur group on a cysteine of the said hydrolase with a genus of targeting moiety comprising any structural and functional features. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6)

the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breath of the claim(s).

Claims 1-5, 8-10,12-29 are so broad as to encompass catalytic antagonist comprising chimeric protein comprising any subtillsin-type serine hydrolase conjugated through the sulfur group on a cysteine of the said hydrolase with a genus of targeting moiety molecule. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of chimeric proteins that made via conjugation of broad class of serine hydrolase conjugated with a broad class of targeting moiety molecules . These claims drawn to chimeric proteins having any structure. In view of the great breaths of claims, amount of experimentation required to isolate specific subtillsin-type serine hydrolase and conjugate any targeting domain molecule to make specific chimeric molecule as catalytic antagonist, the lack of guidance, working examples, unpredictability of the art in predicting the function (hydrolase activity) from protein's structure (Ofran , et al.*Durg discov. Today*. 2005, 10, pp 1475-1482), the claimed invention would require undue experimentation. As such the specification fails to teach one of ordinary skill how to use the full scope of the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the

proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only few chimeric proteins.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only few chimeric proteins of specific amino acid sequences.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass broad class of catalytic antagonist comprising a genus of chimeric protein comprising any subtilisin-type serine hydrolase conjugated through the sulfur group on a cysteine of the said hydrolase with a genus of targeting moiety molecule because the specification does **not** establish: (A) regions of the protein structure which may be

modified without effecting catalytic and inhibitory activity; (B) the general tolerance of serine hydrolase activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues for enzyme activity with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims encompassing a genus of catalytic antagonist comprising chimeric protein comprising any subtilisin-type serine hydrolase conjugated through the sulfur group on a cysteine of the said hydrolase with any of targeting moiety molecule. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of catalytic antagonistic activity of chimeric protein, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Mohammad Meah/

Acting Examiner of Art Unit 1652/1600

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